REMARKS

Claims 20-22, 27, 29-39, 47 and 49-81 are currently pending and presented for examination. Claims 1-19, 23-26, 28, 40-46 and 48 are canceled without prejudice or disclaimer. Applicants reserve their right to prosecute the subject matter of any or all of the canceled claims in one or more continuing applications. Claim 27 is amended to more precisely define the subject matter being claimed. Claims 49-81 are added. Support for each of the claim amendments as well as the new claims can be found throughout the specification and claims as originally filed. In particular, exemplary support for each claim amendment and new claim is set forth in the table provided below. As such, no new matter has been added to the instant application.

Claim Nos.	Independent/Dependent	Amended/New	Exemplary Support
27	Independent	Amended	page 31, lines 16-21 Figures 6A and 6B page 14, lines 29-33 page 6 line 25 to page 7, line 9 page 48, lines 10-17
49-51	Dependent	New	page 48, lines 19-24
52	Dependent	New	page 47, lines 33-34
53, 54	Dependent	New	page 15, lines 11-17
55, 56	Dependent	New	page 15, lines 26-31
57	Dependent	New	page 15, lines 4-9
58	Dependent	New	Examples 2-6 (pages 52-55)
59-61	Dependent	New	page 65, lines 1-11
62	Dependent	New	page 65, lines 5-7
63	Dependent	New	page 65, lines 13-18
64	Independent	New	Page 47, line 25 to page 48, line 29 page 14, lines 10-27
65-67	Dependent	New	page 48, lines 19-24
68	Dependent	New	page 15, lines1-3

Claim Nos.	Independent/Dependent	Amended/New	Exemplary Support
69	Dependent	New	page 47, lines 33-34
70	Dependent	New	page 65, lines 13-18
71, 72	Dependent	New	page 15, lines 26-31
73-80	Dependent	New	page 48, line 26 to page 51, line 18
81	Dependent	New	page 65, lines 5-7

After having carefully considered the Office Action, Applicants respectfully traverse the instant claim rejections. Applicants believe that the arguments presented are persuasive; however, in the event that the Examiner does not agree, Applicants cordially invite the Examiner and her supervisor to resolve any outstanding issues regarding the teachings of the cited art in a personal interview with Applicants and a Patent and Trademark Office subject matter specialist.

Rejection of claims 27, 29-39 and 46 under 35 U.S.C. § 103(a)

The Examiner rejects claims 27, 29-39 and 46 under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 5,837,196 (Pinkel et al.) in view of U.S. Patent No. 5,739,000 (Bierre et al.). In particular, the Examiner asserts that Pinkel et al. disclose arrays having a plurality of subpopulations of sensor elements having identical bioactive agents. The Examiner also asserts that Pinkel et al. disclose contacting such arrays with a target analyte and obtaining response signals from separate sensor elements. The Examiner acknowledges that Pinkel et al. do not disclose statistically analyzing the response signals, however, it is asserted that such analysis would be obvious in view of the disclosure of Bierre et al. Specifically, the Examiner contends that a skilled artisan would incorporate the teachings of Bierre et al. into the methods disclosed by Pinkel et al. because "Pinkel specifically recognized the need for inherent means to calibrate against an internal standard present with an array system (column 1, lines 48-53) and Bierre provided applicability of statistical analysis of data for methods as that taught by Pinkel." Furthermore, the Examiner asserts that statistical analysis is standard laboratory practice that would be obvious to incorporate into the evaluation of the data produced by the claimed methods.

Applicants maintain that each of claims 20-22, 27, 29-39, 46 and 47 are fully patentable over the art of record. There are at least several reasons why Applicants do not agree that the combination of Pinkel et al. and Bierre et al. render any of the above-rejected claims obvious; however, the primary reason for Applicants' disagreement is that the combination of Pinkel et al. and Bierre et al. does not disclose all of the elements of any of these claims. In particular, Pinkel et al. do not disclose obtaining individual response signals from separate sensor elements from at least one of the first and second subpopulations, wherein the sensor elements of the first subpopulation comprise the same bioactive agent, and wherein the sensor elements of the second subpopulations comprise the same bioactive agent (emphasis supplied). Applicants have thoroughly read the instant Office Action and have carefully considered the Pinkel et al. reference in its entirety as well as each specific section that the Examiner cites in support of her contention. In the paragraphs that follow, Applicants address each one of the Examiner's assertions regarding the teachings of Pinkel et al.

In the instant Office Action, the Examiner alleges that the disclosure of Pinkel et al. is not limited to the preferred embodiment, which states that "the detector is preferably arranged to read the signal from single optical fibers **10** or from groups of optical fibers where all of the optical fibers **10** in a group bear the same species of biological binding partner" (see Pinkel et al. at column 9, lines 44-48). Specifically, the Examiner contends that, when viewed in its entirety, in addition to disclosing obtaining signals from groups of optical fibers that bear the same species of biological binding partner, the Pinkel et al. reference also describes obtaining signals from single optical fibers that bear the same species of biological binding partner. In support of this contention, the Examiner recites three specific portions of the Pinkel et al. reference. The first portion recited by the Examiner states the following:

> Alternatively, the transmission ends **12**, may be addressed by attaching the transmission end of each optical fiber **10** or bundle of optical fibers bearing a particular binding partner to an individual detector. Each detector is subsequently known to be associated with a particular biological binding partner and there is no need to preserve a fixed spatial relationship between and of the transmission ends **12**.

(See Pinkel et al. at column 12, line 66 to column 13, line 5).

The above-recited passage, which relates to the attachment of fibers or bundles of fibers to individual detectors, does not disclose an embodiment that differs from the "preferred" embodiment disclosed at column 9, lines 44-48. Rather, this passage, which is parallel in structure to the passage at column 9, lines 44-48, simply states that the transmission end of each optical fiber can be attached to an individual detector, or alternatively, a bundle of optical fibers bearing a particular binding partner can be attached to an individual detector. Because fibers having the same biological binding partner would be expected to emit in the same channel, connecting them all to the same detector would make sense. Thus, taken in context, there is absolutely nothing to support the interpretation that the above-recited passage discloses obtaining signals from separate optical fibers that bear the same biological binding partner.

The second portion of the Pinkel et al. reference set out by the Examiner relates to the use of a charge coupled device (CCD) to read signals generated at the transmission end of the fibers. In particular, the passage states the following:

> Alternatively, a CCD (or other) camera may be focused at the transmission face of the biosensor to simultaeously (sic) read signals from all of the optical fibers while permitting individual evaluation of the signal from each fiber or group of fibers.

(See Pinkel et al. at column 9, lines 37-41).

With respect to the above-recited passage, the Examiner asserts that "Pinkel does not place any regard as to whether each fiber or group of fibers, bears a same or different species of biological binding partner in permitting individual evaluation of the signals obtained." Applicants agree that this passage is silent with respect to biological binding partner. That is precisely why this passage does not disclose obtaining a signal from separate optical fibers when those fibers bear the same biological binding partner. It is well established that a reference

cannot disclose an element that is not described either explicitly or implicitly. As acknowledged by the Examiner, there is no explicit disclosure of obtaining a signal from separate optical fibers when those fibers bear the same biological binding partner. Furthermore, there is no basis in the cited passage, or anywhere else in the Pinkel et al. reference, for inherent disclosure of such a concept. In fact, nearly all of the Pinkel et al. reference discloses obtaining signals from individual fibers that each have different biological binding partners. In the very few instances where obtaining signals from fibers bearing the same biological binding partners is described, it is always with the qualification that such signals are obtained from a group of fibers bearing the same biological binding partners. The Examiner is reminded that an inherent property cannot be established by mere possibilities or probabilities, but rather, the inherent property must be recognized as necessarily present in the described subject matter. This rule regarding inherent disclosure is equally applicable in the context of obviousness as it is in the context of anticipation. *See, In re Grasselli*, 713 F.2d 731, 739 (Fed. Cir. 1983); *In re Napier*, 55 F.3d 610, 613 (Fed. Cir. 1995). Accordingly, at best, Pinkel et al. are silent as to whether signals can be obtained from separate fibers when the fibers contain the same biological binding partner. As discussed below, this silence is insufficient to provide the required disclosure.

Finally, the Examiner recites a third portion of the Pinkel et al. reference that relates to the component structure of the disclosed fiber optic arrays. Specifically, the passage states the following:

> While the single repeating component of the fiber optic biosensor is the individual optical fiber **10**, it is the aggregation of a plurality of such fibers to form a discrete optical fiber array **14** that permits the simultaneous detection of a multiplicity of analytes.

(See Pinkel et al. at column 8, lines 26-30).

This final portion of the Pinkel et al. reference suffers the same deficiency as the passage described above. In particular, Pinkel et al. are silent as to whether signals can be obtained from separate fibers when the fibers contain the same biological binding partner Contrary to the

Examiner's conclusion, this silence is insufficient to provide missing element recited in Applicants' claims. The necessity for an express or inherent disclosure of claim elements is well established in the case law of the Federal Circuit. *See*, *Rowe v. Dror* 112 F.3d 473 (Fed. Cir. 1997). In *Rowe*, the Court remarked "[a]bout the most that can be said for the Lemelson patent is that it does not explicitly describe anything inconsistent with angioplasty procedures. However, this negative pregnant is not enough to show anticipation." *Rowe* 112 F.3d at 480. Although the issue in *Rowe* was whether the claim was anticipated, the same standard applies to the instant obviousness rejection because the Examiner is asserting that Pinkel et al. supply each of the elements of the rejected claims other than performing a statistical analysis. The Examiner relies on obviousness to supply only the statistical analysis element. As a result, Pinkel et al. must disclose each of the claim elements other than the step of statistical analysis. Pinkel et al., however, is silent with respect to at least one of these elements, and thus, it does not provide the required disclosure.

In addition to the foregoing remarks, there is substantial evidence to support the conclusion that Pinkel et al. does not disclose obtaining signals from separate fibers when the fibers contain the same biological binding partner. In particular, Applicants would like to draw the Examiner's attention to column 1, lines 40-63 of the Pinkel et al. reference, which describes the background of their invention. That section states the following:

> Biosensors comprising a biological "binding molecule" attached to an optical fiber are well known in the prior art, most typically as evanescent wave detectors (see, for example, U.S. Pat. No. 4,447,546 to Hirschfeld and U.S. Pat. Nos. 4,582,809 and 4,909,990 to Block et al.). In order to maximize sensitivity and selectivity such biosensors typically utilize a single species of biological binding molecule affixed to the face of the sensor.
>
> Such "single-species" biosensors are limited in that they have no inherent means to correct or calibrate for non-specific binding. Thus, they must be calibrated against an external standard. In addition, they are limited to the detection of a single analyte.

> Biosensors comprising two or more species of biological binding partners overcome these limitations. A "multi-species" biosensor in principle permits simultaneous detection of as many different types of analytes as there are species of biological binding partner incorporated into the sensor. In addition, comparison of the amounts of a single analyte binding to multiple species of binding partner provides a measure of non-specific binding and thus acts as an intrinsic control for measurement variability introduced by non-specific binding.

(See Pinkel et al. at column 1, lines 40-63).

From the above-recited passages, it is clear that Pinkel et al. recognize two deficiencies with respect to the prior art, single-species biosensors. First, single species sensors require external calibration (see lines 49-52). And second, single species biosensors are limited to the detection of a single analyte (see lines 52-53). To overcome these problems, Pinkel et al. contemplate, multi-species biosensors (see lines 54-59). Because Pinkel et al. perceive single analyte detection as problematic, they only contemplate the use of a redundant single binding species when required, such as to amplify signal strength to a detectable level. This explains why the disclosure of Pinkel et al. is limited to obtaining a single signal from a group of fibers that have the same biological binding partner (signal amplification). With respect to the calibration issue, Pinkel et al. contemplate comparing signals obtained from the binding of an analyte with multiple species of binding partner which each recognize that analyte. Thus, the solution to the calibration problem provided by Pinkel et al. does not rely on providing a plurality of copies of the same species of biological binding partner, but rather, it is based on comparative binding by different species of binding partners (different molecules) that recognize the same analyte. Accordingly, in view of their solution to the problems known in the prior art, Pinkel et al. never contemplated arrays where signals from the same species of biological binding partner would be separately obtained. As such, there is absolutely no basis from which to conclude that Pinkel et al. implicitly disclose such an element.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 27, 29-39 and 46 under 35 U.S.C. § 103(a).

Rejection of claims 20-22 and 47 under 35 U.S.C. § 103(a)

The Examiner rejects claims 20-22 and 47 under 35 U.S.C. § 103(a) as allegedly being obvious over Pinkel et al. in view of Bierre et al. and in further view of U.S. Patent No. 5,559,668 (Stimpson et al.). In particular, the Examiner asserts that the combination of Pinkel et al. and Bierre et al. disclose all the elements of claims 20-22 and 47 except for the use of microspheres in the arrays. The Examiner asserts that Stimpson et al. supply this missing element. Furthermore, the Examiner asserts that a skilled artisan would incorporate the beads disclosed by Stimpson et al. into the arrays recited in method claims 20-22 and 47 because Stimpson et al. allegedly teach that the use of such beads increases the speed of data acquisition. As such, the Examiner concludes that the subject matter recited in claims 20-22 would have been obvious to one or ordinary skill in the art.

Applicants respectfully submit that claims 20-22 and 47 are patentable over the art of record. In particular, Applicants submit that the combination of Pinkel et al., Bierre et al. and Stimpson et al. does not teach all of the elements of any one of the above-rejected claims. As discussed in detail above, Applicants maintain that Pinkel et al. does not disclose obtaining individual response signals from separate sensor elements from at least one of the first and second subpopulations, wherein the sensor elements of the first subpopulation comprise the same bioactive agent, and wherein the sensor elements of the second subpopulations comprise the same bioactive agent. None of the other recited references teach this missing element. Accordingly, none of claims 20-22 and 47 are obvious in view of the combination of Pinkel et al., Bierre et al. and Stimpson et al.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 20-22 and 47 under 35 U.S.C. § 103(a).

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or

if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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